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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,070	08/22/2003	Michael Wayne Graham	546322000303	8796

32042 7590 08/28/2006

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,070	GRAHAM ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/27/05, 8/11/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-106* is/are pending in the application.

4a) Of the above claim(s) *92-106* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/100,812,09/646807.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/30/05, 2/28/05, 2/1/06, 7/30/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 48-106 are pending.

The amendment to the claims 48, 49, 51, 53, 77, 82-85, and 102 filed on 8/11/06 has been acknowledged.

The amendment to the specification filed on 12/27/05 has been acknowledged.

The amendment to claims 48, 49, 51, 53, 82-85 filed on 4/7/05 has been acknowledged by the examiner.

The amendment to claims 48, 49, 51, 53, 82-85, and 99 filed on 12/15/04 has been acknowledged by the examiner.

The amendment to the specification and the cancellation of claims 1-47 and the addition of claims 48-106 filed on 12/11/03 is acknowledged and considered by the examiner.

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be to directed to Brian Whiteman, Art Unit 1635.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 12/15/04 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search the product and process of using the product at the same time. This is not found persuasive because of the reasons set forth in the election restriction mailed on 10/15/04. The applicant

does not address the reasons set forth in the election/restriction for why it would be an undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 92-106 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/15/04.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/100,812, filed on 3/20/98 and 09/646,807, 3/19/99.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/100,812, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Instant claim 54 does not have written support under 112 first paragraph for the limitation "stuffer fragment is above about 10 and below about 50 nucleic acids in length".

Instant claims 62 and 63 do not have written support under 112 first paragraph for wherein said region of a genus of target genes is 20 to 30 nucleotides long. The specification of '812 contemplates: "at least about 20-30 nucleotides in length derived from a viral DNA polymerase, viral RNA polymerase, viral coat protein, or visually-detectable gene, more particularly an RNA polymerase gene derived from a virus selected from the list comprising BEV, Sinbis alphavirus, HIV-1, bovine herpes virus and HSV1 or a visually detectable gene which is involved in determining pigmentation, cell death or other external phenotype on a cell, tissue, organ, or organism, amongst others" and "the structural gene component of the synthetic gene comprises at least about 20-30 nucleotides in length derived from the BEV RNA-dependent RNA polymerase gene or the murine tyrosinase gene or the Escherichia coli lac repressor gene lacI or a complementary sequence thereto." See column 6, lines 25-40.

Instant claims 65 and 67 do not have written support under 112 first paragraph for the limitation "viral vector is selected from the group consisting of a retrovirus and a lentivirus".

Instant claim 76 does not have written support under 112 first paragraph for the limitation "the target gene is α-1,3-galactosyltransferase".

Instant claim 77 does not have written support under 112 first paragraph for the limitation "the target gene is beta-1,3-galactosyltransferase".

Instant claims 78-79 and 82-85 do not have written support under 112 first paragraph for the limitation "target gene is derived from the genome of a pathogen of the human cell or the genome of the human cell".

The disclosure of the prior-filed application, Application No. 09/646,807, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Instant claim 54 does not have written support under 112 first paragraph for the limitation "stuffer fragment is above about 10 and below about 50 nucleic acids in length".

The disclosure of the prior-filed application, Application No. 09/646,807, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Instant claim 76 does not have written support under 112 first paragraph for the limitation "the target gene is α-1,3-galactosyltransferase".

Instant claim 77 does not have written support under 112 first paragraph for the limitation "the target gene is beta-1, 3-galactosyltransferase".

Thus, instant claim 77 only has priority to the amendment filed on 12/15/04.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the claim (claim 77) contain new matter that was not in the parent application(s). See MPEP 602.05(a).

Information Disclosure Statement

The examiner has considered the international and European search report and examination reports have been considered, but the reports have not been initialed because they are not considered published documents.

Exhibit A and B have been acknowledged by the examiner. However, the examiner has not considered the references since the 4558 references in Exhibit A or the 270+ references cited in Exhibit B have not been listed on a PTO-1449. The information disclosure statement filed 2/11/05 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The exhibits have been placed in the application file, but the information referred to therein has not been considered.

Specification

The abstract of the disclosure is objected to because part of the abstract that was provided was cut off making it unreadable. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 72-75 and 82-91 are objected to because of the following informalities: the phrase "A(a)n isolated gene construct according to claim" in the claims is an improper phrase for a dependent claim. Suggest replacing "A(a)" with -- T(t)he --.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48-91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New matter rejection:

As stated above, claims 48-91 were new claims filed on 8/22/03 and amended on 12/15/04 and 4/7/05. Applicants did not provide support for the new claims. The examiner thoroughly searched the instant specification and could not find support for the instant claims. Therefore, there does not appear to be a written description of the new claims in the application as filed. See MPEP § 2163.06.

Claims 48-57, 60-67, 72-75, and 78-91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 48-57, 60-67, 72-75, and 88-91, as best understood, is readable on a genus of structural gene sequence comprises a nucleotide sequence which is at least 80% identical to the sequence to the sequence of the target gene or region thereof, wherein the genus of structural gene sequences is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

Claims 78-87, as best understood, is readable on a genus of structural gene sequence comprises a nucleotide sequence which is at least 80% identical to the sequence to the sequence of the target gene or region thereof, wherein the target gene is derived from the genome of a pathogen of the human cell or the genome of the human cell, wherein the genus of structural gene sequences is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

The specification contemplates a target gene which is endogenous to an animal cell or a foreign gene such as a viral or foreign genetic sequence (page 7). The disclosure provides sufficient description for the target gene is α-1,3-galactosyltransferase ~~or β-1,3-galactosyltransforase~~. The specification further provides support for a structural gene component of the synthetic gene comprises derived from the BEV RNA-dependent RNA polymerase gene or the murine tyrosinase gene or the Escherichia coli lac repressor gene lacI. However, the specification does not provide sufficient description of a genus of a structural gene sequence comprises a nucleotide sequence, which is at least 80% identical to the sequence of the target gene or region thereof and is capable of post-transcriptionally delaying, repressing or otherwise reducing the expression of a target gene in a human cell. There is a variation between the species embraced by the claimed genus and function. The specification does not disclose how to

make a representative number of species of the claimed genus with the desired biological function. The prior art does not supplement how to make a representative number of species of the claimed genus with the desired biological function. The skilled artisan would understand that not all sequences embraced by the claimed genus can initiate degradation of target gene or region thereof. It is not apparent that on the basis of the applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the claimed invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of structural gene sequences comprises a nucleotide sequence that must exhibit the disclosed biological functions as contemplated by the specification.

It is not sufficient to contemplate a genus of target gene or region thereof to support the present claimed invention directed to a genus of structural gene sequence comprises a nucleotide sequence which is at least 80% identical to the sequence of the target gene or region thereof. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of structural genes that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient

relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of structural genes that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "is above about 10 and below about 50 nucleic acid in length" in claim 54 line 2 is a relative term, which renders the claim indefinite. The term "is above about 10 and below and about 50 nucleic acid in length" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the limitation are undefined because neither the specification nor the instant claims defined if the nucleic acid length is about 10 or above 10 or about 50 or below 50.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The limitation "capable of post-transcriptionally delaying, repressing or otherwise reducing expression of a target gene in a human cell transfected with the genetic construct by sequence-specific degradation of a RNA transcript of the target gene by an endogenous system of the human cell" in instant claims 48, 49 and 51 and claims dependent therefrom. With regard to the specified activity, if a prior art structure is capable of performing the intended use as recited in the claim, then it meets the claim. See, e.g., In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997).

The term "capable" in the limitation recited in instant claims 48, 49, and 51 and claims dependent therefrom does not require that the construct perform the functions recited in the claimed product.

The limitation "pharmaceutical composition comprising the isolated genetic construct" in instant claims 88-91 does not have patentable weight over the same product taught in the prior art. See MPEP 2111.02.

Claims 48, 50, 58, 60, 62, 64, 68, 70, 72, 74, 78, 80, 82, 84, 86, 88, and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al (US 6,506,559, cited on a PTO-1449). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The promoter can be a T7 and T3 promoters (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). A viral vector can be used as the vector (column 9). The cell can comprise a target gene at risk from a pathogen including HIV (columns 4, 8, and 10). The target gene can be an endogenous from in a human cell (columns 4 and 10-11). The structural gene can comprise one or more strands of the nucleotide sequence (column 4). The vector can be in combination with a carrier (column 14).

Claims 48-52, 55, 58, 59, 62, 63, 72, 73, and 86-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Dorer et al. (Cell, pages 993-1002, 1994, cited on IDS 7/30/04). Dorer et al. teach a synthetic gene comprising a dispersed nucleic acid molecule comprising tandem copies of a nucleotide sequence which is substantially identical to the nucleotide sequence of the mini-white target gene placed operably under the control of a promoter sequence (see especially Figure 3 and the caption thereto). The synthetic gene taught by Dorer et al. thus meets all of the limitations of claims 48-52. Dorer et al. further teach: a synthetic gene comprising tandem inverted and/or direct repeats of a genetic sequence that is endogenous to the genome of an animal (i.e. Drosophila) cell (see especially Table 1) and tandem copies of the nucleotide sequence operably linked to spatially separate promoter sequences (Figure 3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 49, 51, 52, 55, 56, 57, 59, 61, 63, 66, 69, 71, 75, 79, 81, 83, 85, and 87-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with Conrad (US 6,054,299, cited on an IDS filed on 7/30/04). Fire teaches a

vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The promoter can be a T7 and T3 promoters (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). A viral vector can be used as the vector (column 9). The cell can comprise a target gene at risk from a pathogen including HIV (columns 4, 8, and 10). The target gene can be an endogenous from in a human cell (columns 4 and 10-11). The structural gene can comprise one or more strands of the nucleotide sequence (column 4). The vector can be in combination with a carrier (column 14). However, Fire does not specifically teach a construct comprising one promoter operably linked to a nucleotide sequence comprising the sense strand and another promoter operably linked to a nucleotide encoding comprising the antisense strand.

However, at the time the invention was made, Conrad teaches a vector comprising T7 and T3 promoters (Figure 1, Column 7).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Conrad, namely to produce a vector comprising one promoter operably linked to a nucleotide sequence comprising the sense strand and another promoter operably linked to a nucleotide encoding comprising the antisense strand. One of ordinary skill in the art would have been motivated to combine the teaching to isolate either single stranded antisense strand or single stranded sense strand.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 48, 50, 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with Ladner et al (US 5,198,346). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). A viral vector can be used as the vector (column 9). However, Fire does not specifically teach separating a construct comprising the structural gene sequences with a stuffer sequence.

However, at the time the invention was made, Lander teaches using a stuffer fragment having above about 10 nucleotides to introduce a stop codon or a unique restriction site (column and Table 704).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Ladner, namely to produce a construct comprising a structural gene with a stuffer sequence having above about 10 nucleotides. One of ordinary skill in the art would have been motivated to combine the teaching to introduce a termination site after the sense strand or a unique restriction sequence for cloning purposes.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 48, 51, 64, 65, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Fire (US 6,506,559, cited on a PTO-1449) or Fire (US 6,506,559, cited on a PTO-1449) taken with Conrad (US 6,054,299, cited on an IDS filed on 7/30/04). Claims

48, 51, 64, 65, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire as applied to claims 48, 50, 58, 60, 62, 64, 68, 70, 72, 74, 78, 80, 82, 84, 86, 88, and 90 above in the 102(e) or Fire taken with Conrad as applied to claims 49, 51, 52, 55, 56, 57, 59, 61, 63, 66, 69, 71, 75, 79, 81, 83, 85, and 87-91 above in the 103(a), and further in view of Dietz (WO 98/18811, cited on IDS filed on 7/30/04).

However, Fire or Fire taken with Conrad does not specifically teach using a retroviral vector as the viral vector comprising the construct.

However, at the time the invention was made, retroviral vectors were known to one of ordinary skill in the art for delivering a nucleic acid to a cell as exemplified by Dietz (page 16).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire or Fire taken with Conrad in further view of Dietz, namely to produce a retroviral vector comprising the construct. One of ordinary skill in the art would have been motivated to combine the teaching because retroviral vectors can integrate into the genome of a cell and for efficient delivery of the structural gene to the cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 48 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire (US 6,506,559, cited on a PTO-1449) taken with D'Apice et al. (US 6849448). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). However, Fire does not specifically teach a construct comprising a structural gene comprising a

nucleotide sequence which is substantially identical to the sequence of a target gene, wherein the target gene is alpha 1,3-galactosyltransferase.

However, at the time the invention was made, D'Apice teaches, "human pre-formed xenoantibodies play an important role in the hyperacute rejection response in human xenotransplantation (abstract)." "Such epitopes are formed as the result of activity by the enzyme alpha-1,3 galactosyltransferase (abstract)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with D'Apice, namely to produce a construct comprising a structural gene comprising a nucleotide sequence which is substantially identical to the sequence of a target gene, wherein the target gene is alpha 1,3-galactosyltransferase. One of ordinary skill in the art would have been motivated to combine the teaching to study xenoreactivity by inhibition of alpha 1,3-galactosyltransferse in *in vitro* cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 51 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with Conrad (US 6,054,299, cited on an IDS filed on 7/30/04) as applied to claims 49, 51, 52, 55, 56, 57, 59, 61, 63, 66, 69, 71, 75, 79, 81, 83, 85, and 87-91 above, and further in view of Wang et al. (US 20020150968). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). However, Fire does not specifically teach a construct comprising a structural gene comprising a

nucleotide sequence which is substantially identical to the sequence of a target gene, wherein the target gene is beta 1,3-galactosyltransferase.

However, at the time the invention was made, Wang teaches a human melanoma cell line WM266-4, which produces beta 1,3-galactosyltransferase (page 12).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Wang et al., namely to produce a construct comprising a structural gene comprising a nucleotide sequence which is substantially identical to the sequence of a target gene, wherein the target gene is beta 1,3-galactosyltransferase. One of ordinary skill in the art would have been motivated to combine the teaching to study by inhibition of beta 1,3-galactosyltransferse in *in vitro* cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 48-75 and 78-97 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-43, 53-63, and 65 of copending Application No. 10/346,853. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims embrace an isolated genetic construct comprising at least two copies of a structural gene sequence, wherein the structural gene sequence comprise a nucleotide sequence which is identical to at least a region of said target gene, wherein at least two copies of the structural gene sequence are placed under the control of a promoter, wherein one or more copies is placed operably in the sense orientation under the control of at least one promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 48-55, 58-63, 72-75, and 82-91 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27, 38 and 56-64 of copending Application No. 09/646,807. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims embrace an isolated genetic construct comprising at least two copies of a structural gene sequence, wherein the structural gene sequence comprise a nucleotide sequence which is identical to at least a region of said target gene, wherein at least two copies of the structural gene sequence are placed under the

control of a promoter, wherein one or more copies is placed operably in the sense orientation under the control of at least one promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Furthermore, the following serial numbers of co-pending applications contain claims in which an obviousness-type double patenting rejection would be applied:

11/218,999

11/180,928

10/801,191

10/821,726

It is Applicants' burden to file appropriate terminal disclaimers for all relevant applications listed above. Furthermore, if Applicants are aware of any pending applications or patents, which are not listed above, it is Applicants' duty to disclose these applications or patents, and to submit an appropriate terminal disclaimer over these applications or patents as pertinent to the instant invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 48-55, 58-63, 72-75, and 82-91 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 11-15, and 19-22 of U.S. Patent No. 6,573,099. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims embrace an isolated genetic

construct comprising at least two copies of a structural gene sequence, wherein the structural gene sequence comprise a nucleotide sequence which is identical to at least a region of said target gene, wherein at least two copies of the structural gene sequence are placed under the control of a promoter, wherein one or more copies is placed operably in the sense orientation under the control of at least one promoter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

BRIAN WHITEMAN
PATENT EXAMINER